Abstract

Cancer treatment is an integral part of oral and maxillofacial surgery. Oral cancer in particular is a highly prevalent neoplasm. Standard treatment for most of the tumors is radical surgery combined with stage-based neo-/adjuvant therapy. Laser surgery has become a reliable treatment option for oral cancer as well as for precancerous lesions. Widely used lasers in oral and maxillofacial tumor surgery are the CO2 laser, the Er:YAG laser, the Nd:YAG laser and the KTP laser. The use of lasers in tumor surgery has several advantages: remote application, precise cutting, hemostasis, low cicatrization, reduced postoperative pain and swelling, can be combined with endoscopic, microscopic and robotic surgery. However, laser surgery has some major drawbacks: In contrast to conventional incisions with scalpels, the surgeon gets no feedback during laser ablation. There is no depth sensation and no tissue specificity with a laser incision, increasing the risk of iatrogenic damage to nerves and major blood vessels. Future prospects may solve these problems by means of an optical feedback mechanism that provides a tissue-specific laser ablation. First attempts have been made to perform remote optical tissue differentiation. Additionally, real time optical tumor detection during laser surgery would allow for a very precise and straightforward cancer resection, enhancing organ preservation and hence the quality of life for patients with cancer in the head and neck region.

Keywords: laser surgery; laser tumor treatment; oral and maxillofacial surgery; oral squamous cell carcinoma; CO2-laser; Er:YAG-laser, Nd:YAG-laser; KTP-laser; tissue specificity; optical tissue differentiation

1. Introduction

Tumors consistent with a neoplasm exhibit an uninhibited local growth pattern. Benign tumors grow by crowding out. The therapeutic “gold standard” is the surgical enucleation of the tumor tissue. The surrounding healthy tissue can be spared. Semi-malignant and malignant tumors on the other hand invade neighboring tissue structures in a destructive way. Semi-malignant tumors don’t spread through metastasizing. Malignant tumors tend to spread through distant metastases – depending on the stage of the tumor disease, neo-adjuvant or adjuvant radiotherapy and chemotherapy has to supplement the surgical tumor treatment. Radical resection of the tumor tissue is the therapeutic standard for semi-malignant and malignant tumors.
This includes safety margins of 5 mm and up to 15 mm around the tumor tissue, depending on the tumor entity. The term “radical” means that the resection has to comprise all kinds of tissues within the 3-dimensional safety margin – including bone, muscles, major blood vessels and nerve tissue. In the region of the face, neck and oral cavity in particular, this can affect both function and aesthetics. Impaired breathing, swallowing, mastication of food, speech, mimic function, appearance and social integration can severely reduce the quality of life.

Since oral squamous cell carcinoma (OSCC) is one of the ten most common tumors in humans, it is used as an example in the following paradigmatic discussion about laser treatment for tumors in Oral and Maxillofacial Surgery. Alcohol and nicotine are well-known as being causative factors for OSCC. A genetic component seems to be involved as well. OSCC often exhibits a development from normal tissue to increasingly dysplastic cell conglomerates to complete dysplasia with an uninhibited and invasive growth pattern. Dysplastic areas of the oral mucosa may appear as white or red spots with an altered and roughened surface – leukoplaikia and erythroplakia. These altered tissue spots are known to be tumor precursors [1]. Reports on the risk of progression to cancer vary from 6% to 36% [2]. To prevent a complete transformation into a malignant tumor, the precursors are treated preventatively. The most reliable treatment option is the surgical removal of the altered tissue. Aside from excisional surgery with scalpels, electro-coagulation and cryosurgery, laser surgery is widely used for that kind of treatment [3-7].

However, once a malignant tumor has developed from a dysplastic transformation, the preventive character of treatment has to be changed to oncological therapy. As mentioned above, the therapeutic standard is a radical resection of the neoplasm within the 3-dimensional boundaries of safety margins around the tumor tissue, accompanied by stage-based neoadjuvant/adjuvant radiotherapy/chemotherapy. The resection can be performed with traditional scalpel surgery. Other surgical options are high-frequency electrical knives and laser surgery.

Laser surgery provides a variety of advantages for the treatment of tumors in oral and maxillofacial surgery. However, there are different laser wavelengths that provide a diversity of light-tissue interactions. These interactions affect and modulate the advantages of laser surgical treatment. There are disadvantages and drawbacks as well, though. The following is a description of different lasers that are commonly used in oral and maxillofacial surgery, with an outline of the advantages and disadvantages of laser surgery treatment for oral precancerous growth and cancer. The drawbacks of laser surgery in tumor treatment are reviewed from a clinical point of view and possible future solutions and desirable prospects are delineated.

2. Lasers in Oral and Maxillofacial Surgery

The inclusion of lasers in oral and maxillofacial surgery has been in use since the mid-1960s [8]. Lasers have been used as scalpels for tissue removal in the facial region and in the oral cavity [9-13].

Several types of lasers are currently used in oral and maxillofacial surgery. The effects of the laser beam on biological tissue depend on the wavelength of the monochromatic light that can be reflected, scattered or absorbed. Different components of biological tissue absorb light in different wavelength regions, followed by a deposition of energy in the tissue. Surgical lasers in oral and maxillofacial surgery are generally used in two different modes in terms of beam characteristics. On the one hand, the laser can be used in a focused mode, concentrating the energy on a very small region of 0.1-0.5 mm in size. This kind of laser beam is used for incisions and excisions, as a non-contact laser scalpel. On the other hand, the laser can be used in a defocused mode, extending the diameter of the laser beam to approximately 1-5 mm in size. In this mode, the laser beam can be used to exactly ablate superficially spreading tissue areas, layer by layer [14]. This superficial and areal ablation technique is a unique surgical procedure that uses a laser technique for the vaporization of spots detected to be a precancerous growth in the oral cavity [7]. In addition, the total energy that is deposited in the tissue with both modes depends on the time of application and the chosen power, characteristics that are different for each type of laser.

Several types of laser are used in oral and maxillofacial surgery. Depending on the range of their wavelength and their concomitant absorption by biological chromophores, e.g., water and hemoglobin, the lasers are used for different clinical aspects (Fig. 1).
CO2 and Er-YAG-lasers are mainly absorbed by water, resulting in a minimal penetration depth and fast heating, with effective removal of soft and hard tissue. CO2 lasers are mainly used as laser scalpels for the excision of tumors from soft tissues [5, 6, 15, 16]. In a defocused mode, CO2-lasers are used for superficial tissue vaporization, to treat precancerous lesions in the oral cavity [3, 4].

The Er-YAG laser seems to be a highly efficient tool for cutting both soft and hard tissues with minimal damage to the surrounding tissue. However, there are mainly experimental reports on that topic. Reports are still missing with regard to the clinical use of Er-YAG lasers for tumor resection in oral and maxillofacial surgery [17-22].

Nd:YAG lasers emit light at a wavelength range of 1064 nm, which is in-between the absorption maxima of water and blood. The penetration depth is therefore deeper than that of CO2- or Er:YAG lasers and may reach 4 mm, with the possibility of a larger zone of damage to the surrounding tissue. However, due to a higher potency of coagulation, Nd:YAG-lasers are recommended for tissue resection in cases of hemorrhage. Nd:YAG lasers are used for the excision of cancer in a focused mode as well as for the removal of precancerous lesions in a defocused mode. Additionally, they are used solely for coagulation in combination with other lasers or with scalpel excisions [7, 8, 23, 24].

KTP lasers (potassium titanyl phosphate laser) provide light at a wavelength of 532 nm, which is near the absorption maximum of hemoglobin. Hence, KTP-lasers are highly effective hemostatic tools, penetrating the intercellular and intracellular water with minimal absorption or scattering. They are often used for coagulation, but their effectiveness in the treatment of oral precancerous growth and cancer was demonstrated in several clinical trials, especially when used on the highly vascularized tissue of the tongue [25-28]. Other laser may be used for special purposes as well. However, the CO2-laser is currently the most widely used and scientifically validated laser for the vaporization or excision of precancerous stages and invasive neoplasms in oral and maxillofacial surgery.

With regard to tumor resection in oral and maxillofacial surgery, laser excision is meant to be equal to scalpels in terms of completeness and reliability of in sano resection of neoplasms [29, 30]. There are no studies so far that compare different tools, e.g., laser knives, scalpels, electrical cutting devices. Concerning the removal of precancerous growth in the oral cavity, laser excisions as well as laser vaporizations yielded results that were
comparable to scalpel excisions, cryotherapy or electrocauterization in terms of recurrence rates (7.7-38.1%) and malignant transformations after treatment (0.13-17.5%) [3, 7, 31, 32], and provided several advantages at the same time.

3. Advantages of laser surgery in the treatment of oral and maxillofacial tumors

Many advantages are attributed to laser surgery. Laser surgery has a hemostatic effect [8, 9, 33-37]). It was demonstrated that disrupted arteries, veins and lymphatic vessels of up to 500 μm are closed by a CO2 laser beam due to a thermally induced contraction of the collagen in the walls of the vessels [14, 38]. However, the intensity of hemostasis depends on the characteristics and settings of the individual laser surgery system. Hemostasis results in an increased visibility of the surgical site, without the need of further hemostasis or suction devices [5, 39-41]. As a result, some studies were able to demonstrate a reduction of the surgery time for performing tumor surgery in the oral cavity [41, 42]. More extensive comparative studies of up-to-date surgical procedures, regarding the duration of surgery when a laser is used versus a scalpel, are missing so far. Using an electrotome can provide sufficient hemostasis during the tissue cut as well, but electrocontractility of the underlying muscle tissue cause a reduced accuracy of the surgical cut compared to laser resections [36].

Several studies have documented a delayed and reduced intensity of the inflammatory reaction after oral laser surgery compared to conventional scalpel surgery, electrotome or cryosurgery in clinical trials and in vivo animal studies. The reduced inflammation is accompanied by reduced postoperative edema and swelling [37, 43-47]. This is attributed to the inhibition of extravasation of blood and lymph fluid to the surface of the wound [48, 49]. Other studies found an intensified inflammation in laser incisions during the first postoperative week, caused by thermal damage to the surrounding tissue. It was pointed out that the postoperative tissue reactions and healing processes after laser surgery are basically dependant on the characteristics of the laser [49-52].

Laser wounds heal by second intention, no dressing is necessary after the vaporization of superficial lesions [35, 53], no suturing is necessary after tissue excision [5, 6, 39]. Even if laser wounds are left to secondary healing, the pain was found to be significantly lower after a laser resection compared to a scalpel resection with conventional wound care, e.g., dressings or suturing. It is assumed that sealing of the dissected nerve endings modifies the stimulation of pain on the wound surface [34, 37, 41]. One important advantage of laser surgical cutting is the reduced cicatrization. Several studies demonstrated that postoperative tissue contracture after laser excision or laser vaporization is significantly reduced compared to conventional scalpel surgery [8, 33, 41-43, 54]. An in vivo animal study on oral mucosa demonstrated that the elasticity in the region of surgical tissue excision was twice as high after laser surgery compared to scalpel excision [55]. A reduction in the number of myofibroblasts [44, 56, 57] and eosinophils [58] on the wound surface during the healing process after laser surgery is thought to be associated with reduced scar formation. Accordingly, laser surgery demonstrates an improved outcome with regard to the mobility of the soft tissues, with less oral dysfunction compared to conventional surgical methods [4, 59-61] (Fig. 2-5).

The mobility of the tongue in particular has a major impact on speech production and swallowing, two essential parameters of quality of life [62]. Another factor of cancer treatment is the control of neoplastic cells during surgery. Laser surgery is meant to diminish the risk of disseminating neoplastic cells during the treatment, due to the above-mentioned sealing of blood and lymphatic vessels through thermal effects, reducing the risk of tumor cells being introduced into the body’s fluid circulation [34, 40, 53, 63]. However, to date there have been no randomized long-term studies concerning distant metastases after laser tumor resection in the oral cavity.
Fig. 2. Squamous cell carcinoma on the floor of the mouth

Fig. 3. One day after laser excision of a squamous cell carcinoma on the floor of the mouth

Fig. 4. Six month after laser ablation of a squamous cell carcinoma on the floor of the mouth
Fig. 5. Two years after laser ablation of a squamous cell carcinoma on the floor of the mouth

4. Disadvantages of laser surgery in the treatment of oral and maxillofacial tumors

One disadvantage of laser surgery is represented by the histological evidence of a thermal alteration around the zone of laser tissue ablation. Thermal alterations may range from transient heating to protein denaturation, evaporation of water, carbonization or complete thermal destruction in terms of tissue burning [48, 49, 64]. Several laser parameters have an impact on the extent of the thermal alteration: the wavelength of the laser beam, power setting, continuous/pulsed mode, duration of the laser pulse, frequency of the laser pulse and total exposure time [46, 50, 65, 66]. Additionally, the composition and architecture of the laser-treated tissue [67] as well as amount of blood circulation influence the thermal effects of laser ablation [8]. It is assumed that the thermal damage around the laser incision/ablation is responsible for a delayed healing process compared to a scalpel incision. This mainly applies to the first 7 days of wound healing with regard to histological and biochemical parameters [50] and coincides with delayed inflammation - as mentioned above - and delayed revascularization [45]. Furthermore, some studies indicate that the re-epithelialization is slowed in laser surgery wounds [39, 44]. However, this may only be the case during the first days of healing. In vivo animal and clinical studies were able to demonstrate an equal state of wound healing for undressed and non-sutured wounds after scalpel and laser surgery after 10 to 14 days [50, 66]. A complete wound closure was found 4 weeks after surgery, applying equally to scalpel, laser and electrosurgical wounds [46].

Another problem is related to the thermal alteration of tissue around the laser incision. In tumor surgery, the histological assessment of the tumor tissue is mandatory and essential. This refers to the primary diagnosis prior to any therapy as well as to the evaluation of the resection margins in terms of a complete resection of all tumor tissue. It is stressed that this “gold-standard” should be applied not only in cases of suspected carcinoma, but also with all cases of precancerous oral growth [6, 68]. Some authors suggest a complete excision of precancerous lesions, followed by a histological examination [69]. However, the excision technique by scalpel or laser may be difficult with widespread and multi-focal lesions. Laser vaporization turned out to be a beneficial and reliable tool for those types of lesions [3, 7]. Still, even after a scalpel biopsy prior to laser vaporization, there is a factor of uncertainty without the option of a complete histological examination of the precancerous tissue.

Additionally, it was assumed that the alteration of the tissue through the laser ablation prevented an exact histological assessment, affecting both the primary diagnosis and the safety margins of resected tumor tissue. A morphological, histochemical and immunocytochemical study described blisters, clefts and erosions of the epithelium, intracellular edema, elongated nuclei and a decrease in the glycogen content in CO² laser biopsies [22]. However, these kind of artifacts do not seem to affect a proper histological assessment [Matsumoto, 2008 #82; Tuncer, 2009 #84], if the safety margins are wide enough for a reliable histological evaluation, without the interference of thermally altered tissue areas [70].

One major drawback that limits the surgical application of lasers is the lack of haptic feedback during laser surgery. Performing laser surgery with tissue penetration that exceeds the superficial layer, the surgeon receives no information about the actual ablation depth or information about the ablated tissue at the bottom of the cut. Therefore, in cases that involve a complex anatomy of the surgical area, the use of lasers involves the risk of
iatrogenic damage or destruction of structures that should be preserved, e.g., blood vessels and nerves [71-75]. In the head and neck area, this particularly concerns sensory and motor function nerves. Their damage may immensely affect both function and aesthetics.

Minor disadvantages of laser surgery are on the technical side. For safety reasons, eye protection is necessary for the patient and the surgeon. Most of the laser surgery systems are bulky, which particularly limits their use in the narrow space of the oral cavity. Additionally, there is still no flexible light guide for a variety of lasers. However, there have been advances in the endoscopic use of CO2-lasers with flexible optics [76, 77]. Most of the laser surgery systems have no option for switching between different wavelengths, thereby limiting the utilization of the complete variety of clinical laser effects.

5. Future developments and prospects

Tissue treatment via laser light provides various advantages that may allow laser surgery to become an essential and standard surgical tool in oral and maxillofacial surgery, as well as for surgery in general. Of course, this applies not only to tumor surgery but can be extrapolated to all other surgical treatment entities. However, there are several drawbacks that require a solution or optimization in the future.

From surgical practitioner’s point of view, smaller laser surgery devices are preferable. Bulky devices with lever arms are always a hindrance in the operating theatre. A lot of patients that have to be treated due to pathological alterations in the oral cavity have a diminished ability to open their mouth. Hence, the surgical treatment approach is difficult. This applies to all kinds of surgical tools, including classical scalpel treatment. Laser surgery hand pieces that are reduced in size and have flexible light guides for all kinds of laser beam wavelengths could deliver a proper solution for this problem from a technical aspect [76, 78].

In general, the possibility of combining laser surgery with other technical devices will establish new surgical treatment options. Endoscopic surgery immensely benefits from optical tissue treatment, providing solutions for minimally invasive surgery that has been limited by the mechanical nature of classical instrumentation [59, 60, 79]. Additionally, first attempts to combine oral laser surgery with robotics in experimental and preliminary clinical trials [80-82] as well as 3-dimensional surgical guidance consistent with automated surgery [83-85] have yielded positive results.

Biological tissue modulates light in a specific way. Absorption, reflection, refraction, fluorescence and optoacoustic reactions are followed by a tissue-specific change of the optical spectra that is used for the control of laser surgical processes [21, 86-92]. In addition, optics provide the possibility of remote tissue characterization and differentiation. Several studies were able to demonstrate a sufficient optical identification of pathologically altered tissue, e.g., cancerous tissue [93-97]. Additionally, first successful attempts have been made in remote optical differentiation of normal soft and hard tissue types [98-100]. The laser ablation of biological tissue produces optical and optoacoustic process emissions. These emissions were used experimentally to identify the ablated tissue and for laser ablation monitoring/guidance by means of a closed loop feedback system [87-89, 101].

Based on these optical tissue differentiation methods, tissue-specific laser surgery could be developed, overcoming several problems in conventional and laser surgery for the treatment of tumors: Tissue-specific feedback monitoring/guidance of the laser cut will reduce the risk of iatrogenic tissue damage, especially to nerves or major blood vessels, enhancing the safety of laser surgery. The possibility of an intra-operative optical biopsy for the detection of malignant tissue will dramatically enhance the quality of tumor resections. The surgery time will be sped up while the surgical resection will be performed with higher precision. Optical real-time monitoring of the tumor removal will overcome the problem of intra-operative identification of the lateral tumor margins and the depth of the tumor expansion. Removing the tumor tissue according to a continuous optical detection of dysplastic cells will provide a maximum of exactness and hence of organ preservation, which will be highly beneficial for patients with oral cancer.

References